State of California—Health and Human Services Agency
Department of Health Care Services

RICHARD FIGUEROA
ACTING DIRECTOR

GAVIN NEWSOM
GOVERNOR

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TO: All County California Children's Services Program Administrators, Medical Consultants, and Integrated Systems of Care Division Staff

SUBJECT: Tisagenlecleucel (Kymriah) – Revised

I. PURPOSE

The purpose of this Numbered Letter (N.L.) is to update California Children's Services (CCS) Program policy regarding the authorization of tisagenlecleucel (Kymriah). Tisagenlecleucel is a treatment for B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse, and for treatment of large B-Cell lymphoma that is refractory or relapsed after two or more systemic therapies. This includes diffuse large B-Cell lymphoma (DLBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. Specifically, this N.L. broadens the approved CCS indications for the use of tisagenlecleucel to align with expanded the federal Food and Drug Administration (FDA) approved indications to include certain B-cell lymphomas.[1]

II. BACKGROUND

ALL is a cancer of the blood and bone marrow characterized by the development and proliferation of large numbers of immature lymphocytes. ALL arises from malignant transformation of progenitor B-cells or T-cells in the bone marrow into leukemic cells. It is characterized by the accumulation of lymphoblasts in the bone marrow or in various extramedullary sites.[2] ALL is the most common cancer in children and represents 25 percent of cancer diagnoses in children younger than 15 years of age.[3] Every year, ALL is diagnosed in approximately 3,100 children age 20 years or younger.[4] B-cell leukemia is the most common form of ALL.

Non-Hodgkin's Lymphoma (NHL) is a cancer that arises from lymphocytes, specifically B-cells, T-cells, or natural killer cells. Risk factors for NHL in childhood include: past treatment for cancer, infection with Epstein-Bar virus or human immunodeficiency virus, a weakened immune system, and having an inherited condition with impaired DNA repair mechanisms.

The FDA approved tisagenlecleucel on August 30, 2017, as the first in class of chimeric antigen receptor T-cell therapy (CAR-T) for individuals up to 25 years of age with B-cell precursor acute lymphoblastic leukemia that is refractory or in second or later relapse. Tisagenlecleucel suspension is a Cluster of Differentiation 19 (CD19)-directed genetically modified autologous T-cell immunotherapy. This involves reprogramming a patient's own T-cells with a transgene encoding a chimeric antigen receptor (CAR) to identify and eliminate CD19-expressing malignant and normal cells.

When the CAR binds to CD19-expressing cells, it sends a signal to reprogram other T-cells. This leads to expansion, activation, and ultimately, elimination of the non-CAR positive T-cells and persistence of the CAR-positive T-cells.

The CAR-T process involves the following steps:

A. Leukapheresis.

B. Cryopreservation and sending cells to the manufacturer.

C. Programming of the cells.

D. Return of the programmed CAR-T cells to the treatment center.

E. Preparation of the client with lymphodepleting chemotherapy.

F. Infusion of the CAR-T cells.

III. POLICY

Effective the date of this letter, tisagenlecleucel is a CCS Program benefit when the following criteria are met:

A. The CCS client meets the CCS Program residential, financial, and medical eligibility criteria.

B. The client has a diagnosis of:

1. B-cell precursor ALL that is refractory or in second or later relapse, for clients up to age 21, or

2. Large B-cell lymphoma refractory or relapsed after two or more systemic therapies, including relapsed or refractory DLBCL, not otherwise specified, high grade B-cell lymphoma, or DLBCL arising from follicular lymphoma[5]

C. The client is under the care and monitoring of a CCS Program paneled physician at a CCS-approved hematology/oncology Specialty Care Center (SCC) that has all of the following:

   1. Accreditation by the Foundation for the Accreditation of Cellular Therapy (FACT) for immune effector cell therapy.

   2. Current Risk Evaluation and Mitigation Strategy (REMS) certification, known as Kymriah REMS, including the use of tocilizumab for cytokine release syndrome, if it occurs.

D. The request for administration of tisagenlecleucel is aligned with current FDA guidelines:

   1. For clients with ALL:

      a. Indication: client has B-cell precursor ALL that is refractory, or in second or later relapse.

      b. Dosage: for clients 50 kg or less, administer 0.2 to 5.0 x 10^6 total CAR-positive viable T-cells per kg body weight intravenously and for clients above 50 kg, administer 0.1 to 2.5 x 10^8 total CAR-positive viable T-cells (non-weight based) intravenously.

      c. CCS clients of all ages are eligible for tisagenlecleucel treatment of ALL.

   2. For clients with B-cell lymphoma:

      a. Indication: large B-cell lymphoma refractory or relapsed after two or more systemic therapies; DLBCL, high grade B-cell lymphoma, or DLBCL arising from follicular lymphoma.

      b. Dosage: administer 0.6 to 6.0 x 10^8 total CAR-positive viable T-cells intravenously.

      c. CCS clients age 18 years and older are eligible for tisagenlecleucel treatment of B-Cell lymphoma.

E. The client is assigned one of the following ICD-10-CM codes:

   1. C91.00, Acute lymphoblastic leukemia not having achieved remission.

   2. C91.02, Acute lymphoblastic leukemia, in relapse.

   3. C83.30 – C83.39, Diffuse large B-cell lymphoma.

4. C85.20 – C85.29, Mediastinal (thymic) large B-cell lymphoma.

F. If the criteria described above are not met, but the requesting provider has clinical documentation and/or scientific evidence that may be relevant to the request, the provider may submit this additional documentation to the ISCD Medical Director or designee for consideration during the medical eligibility determination.

IV. POLICY IMPLEMENTATION

A. Tisagenlecleucel is not covered by a Service Code Grouping authorization and a separate Service Authorization Request (SAR) is needed. Tisagenlecleucel is carved out of hospital diagnosis related group reimbursement and therefore SCC authorization to an outpatient provider is required even when the drug is administered on an inpatient basis.

B. For non-Whole Child Model (WCM) independent counties, requests for Tisagenlecleucel will be reviewed and authorized by county CCS Programs.

C. For dependent counties, requests for tisagenlecleucel will be reviewed and authorized by the Integrated Systems of Care Division (ISCD) Special Populations Unit at CCS_Operations@dhcs.ca.gov, or to secure RightFax number,
(916) 440-5768.

D. For WCM counties, requests for tisagenlecleucel will be reviewed and authorized by the Managed Care Plan (MCP) and requests for authorization should be directed to the appropriate county-specific MCP authorization unit.

E. Requesting CCS providers must submit:

1. A CCS Program SAR along with:

a. A copy of the prescription or of an order signed by a physician who is CCS-paneled and is associated with a CCS Program approved hematology/oncology SCC.

b. Progress notes from the SCC within the past 90 days documenting:

(1) Status of ALL or B-cell lymphoma.

(2) Latest relevant laboratory values.

(3) Past ALL or B-cell lymphoma treatments, if any.

(4) No active infection at the time of the SAR submission.

(5) No active inflammatory disorder(s) at the time of the SAR submission.

c. Documentation establishes that the SCC has:

(1) FACT accreditation for immune effector cell therapy.

(2) REMS certification, known as Kymriah REMS.

(3) The drug tocilizumab is available to use if needed for treatment of cytokine release syndrome, a potentially life-threatening complication of tisagenlecleucel treatment.

(4) Supportive care if needed.

F. The treating hematology/oncology SCC must bill tisagenlecleucel using the UB-04 claim form.

G. Providers must submit the invoice from the manufacturer for tisagenlecleucel with their claim.

H. The treating hematology/oncology SCC must bill with Healthcare Common Procedure Coding System code Q2042:

1. Q2042 = Tisagenlecleucel, up to 600 million (or 6 x 10^8) CAR-positive viable T-cells. Beginning 1/1/2019.

2. Approval for Q2042 is limited to one unit.

If you have any questions regarding this N.L., please contact the ISCD Medical Director or designee, via email at ISCD-MedicalPolicy@dhcs.ca.gov.

Sincerely,

ORIGINAL SIGNED BY

Roy Schutzengel
Medical Director
Integrated Systems of Care Division

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[1] https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/kymriah-tisagenlecleucel
[2] https://www.cancer.gov/types/leukemia/hp/adult-all-treatment-pdq
[3] https://www.cancer.gov/types/leukemia/hp/child-all-treatment-pdq#cit/section_1.5
[4] FDA News Release: FDA Approval Brings First Gene Therapy to the United States, August 30, 2017
https://www.fda.gov/news-events/press-announcements/fda-approval-brings-first-gene-therapy-united-states
[5] https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/kymriah-tisagenlecleucel